

Attorney Docket No.: BERN-0040
Inventors: Bernstein et al.
Serial No.: 09/913,697
Filing Date: January 28, 2002
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REMARKS

At the outset, Applicants wish to thank Examiner George for the courtesy of the Interview conducted on January 28, 2003.

Claims 1-10 are pending in the instant application. The rejection of claims 1-10 under 35 U.S.C. § 102(e) as being anticipated by Lezdey et al. (U.S. Patent 6,096,327) has been maintained. The Rule 131 Declaration filed by Applicants on September 4, 2002 showing prior conception and reduction to practice of the instant claimed invention prior to the filing date of Lezdey et al. was not found convincing as it was unclear to the Examiner what composition was being used and whether the animal model was protected from photoaging, sunburn and skin cancer by applying the serine protease inhibitor composition.

Accordingly, as discussed with Examiner George at the Interview conducted January 28, 2003, Applicants are submitting a new Rule 131 Declaration herewith evidencing both conception and reduction to practice of methods and compositions for protecting skin exposed to sunlight against photoaging, sunburn and skin cancer via topical application of a serine protease inhibitor or milk.

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As discussed in paragraph 2 of Dr. Bernstein's Declaration and evidenced by laboratory notebook page 68 attached to the Declaration as Exhibit A, the inventors conceived of the idea of using anti-elastase serine protease inhibitor alpha-1-antitrypsin to prevent skin photoaging. Further, they discussed modes of formulation and application, as well as use of a mouse model expressing human elastin promoter-chloramphenicol to test their concept. See paragraph 2 of Dr. Bernstein's Declaration. Further, as made clear by Dr. Bernstein's statement in paragraph 3, the inventors' conception and recordation of this invention at laboratory notebook page 68 occurred prior to the November 5, 1998 filing date of the U.S. Patent 6,096,327.

Accordingly, the inventors of the instant application conceived of the claimed invention prior to the filing date of U.S. Patent 6,096,327.

Further, as discussed in paragraph 4 of Dr. Bernstein's Declaration and evidenced by laboratory notebook pages 1-3 attached to the Declaration as Exhibit B, the inventors conducted in vivo experiments demonstrative of the ability of the serine protease inhibitor alpha-1-antitrypsin to protect skin exposed to sunlight against photoaging, sunburn and skin cancer. Experiments were performed in an established mouse model, the

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results of which correlate with photoaging and DNA damage (such as that caused by sunburn and skin cancer) in humans (see paragraph 4 of Dr. Bernstein's Declaration). In these experiments, an optimal formulation comprising milk from two different transgenic goats, D-161 and D-174, each producing the serine protease inhibitor alpha-1-antitrypsin, in different concentrations was developed in Lubriderm (see paragraph 4 of Dr. Bernstein's Declaration and laboratory notebook pages 1-3 attached as Exhibit B). A 2 mg/cm² formulation comprising a 1:1 ratio of Lubriderm to transgenic goat's milk was applied to the backs of transgenic mice and the mice were exposed to either 10 MEDs of solar-simulating light or 20 MEDs of solar-simulating light (see paragraph 4 of Dr. Bernstein's Declaration and laboratory notebook pages 1-3 attached as Exhibit B). The 20 MED solar-simulating light dose was found to be an optimal dose causing a 21.5-fold increase in elastin promoter activity in untreated transgenic mice exposed to the light (see paragraph 4 of Dr. Bernstein's Declaration). Transgenic mice treated with Lubriderm formulations comprising milk from goat D-161 or goat D-174 prior to light exposure exhibited decreased levels of promoter induction of 11.3-fold and 16.4-fold, respectively (see paragraph 4 of Dr. Bernstein's Declaration).

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Thus, this experiment, performed prior to the November 5, 1998 filing date of U.S. Patent 6,096,327 (see paragraph 5 of Dr. Bernstein's Declaration) showed the ability of alpha-1-antitrypsin to protect against elastin promoter damage and is indicative of the ability of serine protease inhibitors to protect the skin against photoaging, sunburn and skin cancer (see paragraph 4 of Dr. Bernstein's Declaration). Accordingly, the invention as set forth in independent claims 1, 5 and 8 and claims dependent therefrom was reduced to practice prior to the filing date of U.S. Patent 6,096,327 as well.

As discussed in paragraphs 6 and 7 of Dr. Bernstein's Declaration, additional experiments confirming the effectiveness of serine protease inhibitors in protecting skin exposed to solar-simulating light from photodamage, sunburn and skin cancer and demonstrating the ability of milk alone to protect skin exposed to sunlight from photodamage, sunburn and skin cancer were also performed prior to the November 5, 1998 filing date of U.S. Patent 6,096,327. Results from these experiments are depicted in the Figure attached to Dr. Bernstein's Declaration as Exhibit C.

Thus, as shown by the Declaration of Dr. Bernstein and the evidence attached thereto, Applicants conceived and reduced to

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practice the invention of protecting skin exposed to sunlight from photodamage, sunburn and skin cancer using a serine protease inhibitor prior to the November 5, 1998 filing date of U.S. Patent 6,096,327. As also shown by Dr. Bernstein's Declaration and the evidence attached thereto, Applicants conceived of and reduced to practice both the methods as set forth in independent claims 1 and 5 of the instant application and the compositions as set forth in independent claim 8 of the instant application prior to the November 5, 1998 filing date of U.S. Patent 6,096,327.

Further, Applicants demonstrated the utility of their invention using a well-established, scientifically-based, patented model for photodamage, sunburn and skin cancer, and not a simple visual examination of 5 adults from which the impossible result of a reduction in wrinkles in only one week is alleged (see column 7, line 20 through column 8, line 2 of U.S. Patent 6,096,327).

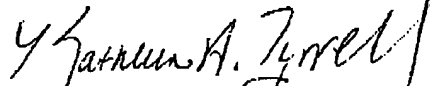
Therefore, U.S. Patent 6,096,327 is not a valid reference with respect to the instant application and withdrawal of this rejection under 35 U.S.C. § 102(e) is respectfully requested.

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CONCLUSION

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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